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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/478,621	01/05/2000	Stephen E. Epstein	674522-2001	1917

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FROMMER LAWRENCE & HAUG  
745 FIFTH AVENUE- 10TH FL.  
NEW YORK, NY 10151

EXAMINER

JIANG, DONG

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 08/20/2002

16

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action**

Application No.

09/478,621

Applicant(s)

EPSTEIN ET AL.

Examiner

Dong Jiang

Art Unit

1646

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 09 August 2002 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY** [check either a) or b)]

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on \_\_\_\_\_. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
  - (b) ☐ they raise the issue of new matter (see Note below);
  - (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
  - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_

3. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_

Claim(s) objected to: \_\_\_\_\_

Claim(s) rejected: 1,3-5 and 8-11.Claim(s) withdrawn from consideration: 12-17.

8. ☐ The proposed drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_
10. ☐ Other: \_\_\_\_\_

  
LORRAINE SPECTOR  
PRIMARY EXAMINER

Continuation of 3. Applicant's reply has overcome the following rejection(s): the rejection of claims 5 and 9-11 under 35 U.S.C. 112, second paragraph, and the rejection of claims 1, 3-5 and 8-11 under 35 U.S.C. 112, first paragraph.

Continuation of 5. does NOT place the application in condition for allowance because: the prior art rejection of claims 1, 3-5, and 8-11 under 35 U.S.C. 103(a) as being unpatentable over Inoue et al. (Circulation, Nov. 1998, 98(20): 2108-16), and Maisonpierre et al. (Science, July 1997, 277:55-60), in view of Kendall et al. (US 5,712,380), and Asahara et al. (Circ. Res., 1998, 83: 233-240), is maintained for reasons of record set forth in the previous Office Actions, paper Nos. 9 and 13, and the reasons below.

Applicants argument has been fully considered, but is not deemed persuasive because, while applicant indicates what each reference does not teach, the cited references in combination render the instant invention obvious.

In particular, it is known in the art that angiogenesis occurs in human coronary atherosclerosis, and Inoue further demonstrates the presence of microvessels in atherosclerotic plaques. In addition, Inoue teaches the involvement of VEGF in atherosclerosis, and VEGF is a key mediator of neovascularization associated with a variety of disorders.

Kendall teaches a soluble VEGFR useful for treatment of pathological angiogenesis present in a variety of disorders and conditions besides tumor growth. Such conditions would include atherosclerosis.

Maisonpierre teaches that ang-2 can antagonize the effect of ang-1 on vessel maturation and stabilization, and that therapeutic manipulation of vessel growth is likely to require simultaneous regulation of both VEGF and angiopoietin systems.

Asahara teaches that ang-2 + VEGF promote neovascularity, indicating inhibiting both would reduce neovascularity.

Therefore, the cited references in combination provide clear logic for one of ordinary skill in the art to make a composition as claimed, and use it in a method of treating atherosclerosis or restenosis as claimed.

Continuation of 7: the rejection of claims 1, 3-5, and 8-11 under 35 U.S.C. 103(a) is maintained for reasons set forth in item 5 above.